WE CLAIM:

1. A chimeric antisense oligonucleotide comprising: a 5' terminus; a 3' terminus and from 11 to 59 5'→3'-linked nucleotides capable of contiguously hybridizing to a specific RNA and independently selected from the group consisting of 2'-modified phosphodiester nucleotides, and 2'-modified P-alkyloxyphosphotriester nucleotides; and wherein said 11 to 59 5'→3'-linked nucleotides are divided by an RNase H-activating region capable of contiguously hybridizing to the specific RNA and of between three and ten contiguous phosphorothioate-linked deoxyribonucleotides, and wherein the 3' terminus of said oligonucleotide is drawn from the group consisting of: an inverted deoxyribonucleotide, a contiguous stretch of one to three phosphorothioate 2'-modified ribonucleotides, a biotin group, and a P-alkyloxyphosphodiester nucleotide, and wherein the 5' terminus of said oligonucleotide is drawn from the group consisting of: an inverted deoxyribonucleotide, a contiguous stretch of one to three phosphorothioate 2'-modified ribonucleotides, a biotin group, and a P-alkyloxyphosphodiester nucleotide.

2. The oligonucleotide of claim 1, provided the 3' terminus is not blocked by a 3'→3' phosphorothioate linked nucleotide.

3. The oligonucleotide of claim 1, in which the 3' terminus is blocked by a moiety comprising a 3'→3' phosphorothioate linked nucleotide.

4. The oligonucleotide of claim 1, in which the 3' terminus is blocked by a moiety comprising a 3'→3' phosphodiester linked nucleotide.

5. The oligonucleotide of claim 4, in which the 3' most 5'→3' internucleotide linkage is a phosphorothioate linkage or a P-ethoxyphosphotriester linkage.

6. The oligonucleotide of claim 4, in which the 5' most 5'·3' internucleotide linkage is a phosphorothioate linkage or a P-ethoxyphosphotriester linkage.

7. The oligonucleotide of claim 1, in which the 3' terminal nucleoside and the 5' most nucleotide are 2'-modified nucleotides.

8. The oligonucleotide of claim 7, in which the 5' most 5'·3' internucleotide linkage is a phosphorothioate linkage or a P-ethoxyphosphotriester linkage.

9. The oligonucleotide of claim 8, in which the two 5' most 5'→3' internucleotide linkages are independently either a phosphorothioate linkage or a P-ethoxyphosphotriester linkage.

10. The oligonucleotide of claim 8, in which all phosphorothioate linkages are contiguous with the 3' most 5'→3' internucleotide linkage.

11. The oligonucleotide of claim 10, in which the 2'-modified nucleotide is a 2'-methoxy or 2'-fluoro nucleotide.

12. The oligonucleotide of claim 10, which comprises at least thirteen 2'-methoxy phosphodiester nucleotides.

13. The oligonucleotide of claim 10, having between 15 and 50 nucleotides.

14. The oligonucleotide of claim 13, which comprises at least eight 2'-methoxy phosphodiester nucleotides.

15. The oligonucleotide of claim 13, which comprises at least thirteen 2'-methoxy phosphodiester nucleotides.

16. The oligonucleotide of claim 1, in which the 2'-modified nucleotides are selected from the group consisting of 2'-fluoro and 2'-methoxy nucleotides.

17. The oligonucleotide of claim 1, in which there are no 2'-modified phosphorothioate nucleotides.

18. A method of specifically cleaving an RNA in a cell containing RNase H which comprises administering an effective amount of an oligonucleotide complementary to the RNA comprising: a 5' terminus; a 3' terminus; and from 11 to 59 5'→3'-linked nucleotides capable of contiguously hybridizing to the RNA and independently selected from the group consisting of 2'-modified phosphodiester nucleotides, 2'-modified P-alkyloxyphosphotriester nucleotides; and wherein said 11 to 59 5'→3'-linked nucleotides are divided by an RNase H-activating region capable of contiguously hybridizing to the RNA and of between three and ten contiguous phosphorothioate-linked deoxyribonucleotides, and wherein the 3' terminus of said oligonucleotide is drawn from the group consisting of: an inverted deoxyribonucleotide, a contiguous stretch of one to three phosphorothioate deoyribonucleotides, phosphorothioate 2'-modified ribonucleotides, a biotin group, and a P-alkyloxyphosphodiester-linked nucleotide, and wherein the 5' terminus of said oligonucleotide is drawn from the group consisting of: an inverted deoxyribonucleotide, a contiguous stretch of one to three phosphorothioate deoyribonucleotides, phosphorothioate 2'-modified ribonucleotides, a biotin group, and a P-alkyloxyphosphodiester-linked nucleotide.

19. A chimeric antisense oligonucleotide comprising:

a) an RNase H activation region capable of contiguously hybridizing to a specific RNA and having between 5 and 10 contiguous deoxyphosphorothioate nucleotides;

b) between 4 to 59 contiguous 5'-3'-linked 2'-methoxy ribonucleotides capable of contiguously hybridizing to the specific RNA;

c) an exonuclease blocking group present at the 3' end, the 5' end, or both the 3' and 5' ends of the oligonucleotide drawn from the group consisting of: a non-5'-3' phosphodiester-linked nucleotide, from one to three contiguous 5'-3'-linked modified nucleotides, and a non-nucleotide chemical blocking group.